REMARKS

1. Preliminary Matters

Claims 65-77 are pending in this application. An Amendment and Reply under 37 C.F.R. § 1.113 filed on June 8, 2005 (the "First Reply") was not entered by the Examiner as indicated in the Advisory Action mailed July 6, 2005 (the "Advisory Action"). Applicant herein resubmits only those claim amendments presented in the First Reply that address the outstanding rejection under 35 U.S.C. § 112, second paragraph.

Claims 66 and 78-81 are herein cancelled without prejudice to pursuing similar or identical claims in a continuing application. Claims 1-64 were previously cancelled. Claims 68-77 have been amended. Upon entry of these amendments, claims 65 and 67-77 are pending and under active consideration. Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present application.

Claims 68-77 have been amended to correct claim dependency necessitated by the cancellation of claim 66. Accordingly, Applicant respectfully submits that no new matter has been added.

2. Rejections

a. 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claim 66 as vague based on the phrase "variant, analog and derivative of the sequence set forth in SEQ ID NO:4," and has further rejected claims 70-77 as indefinite due to their dependence on claim 66. Applicant respectfully submits that claim 66 has been cancelled and claims 70-77 have been amended to remove dependency to cancelled claim 66. Applicant therefore respectfully submits that the rejection under 35 U.S.C. § 112, second paragraph has been overcome.

b. 35 U.S.C. § 102(b)

The Examiner maintains the rejection of claims 65-77 under 35 U.S.C. § 102(b) for lack of novelty in view of O'Brien and Yang. At page 9 of the Office Action mailed October 6, 2004 (the "First Office Action"), the Examiner characterizes the antibodies of the cited references as having "identical functional properties" to the claimed antibodies. At page 9 of the First Office Action, the Examiner also characterizes O'Brien and Yang as each teaching antibodies that bind to Cyr61. At page 9 of the First Office Action, the Examiner alleges that based on extensive

homology of Cyr61 across species, antibodies that bind human Cyr61 would likely bind Cyr61 homologs from other species. At page 9 of the First Office Action, the Examiner requires Applicant to demonstrate that the antibodies disclosed in the cited references do not have the same characteristics of the claimed antibodies.

In response to the First Office Action, Applicant submitted that the Examiner had failed to consider each and every element of the claims. At page 6 of the Amendment and Reply Under 37 C.F.R. § 1.111 filed January 6, 2005, Applicant noted that the antibodies described in O'Brien and Yang were raised to mouse Cyr61 not human Cyr61. As such, Applicant argued that the antibodies of O'Brien and Yang cannot bind *specifically* to human Cyr61. In response to Applicant's arguments, the Examiner states at page 6 of the Final Office Action that "[i]t appears that what is at issue is that the references do not specifically teach that the disclosed antibodies that react with cyr61 will specifically react with the cyr61 set forth in SEQ ID NO:4." At pages 6-7 of the Final Office Action, the Examiner alleges that there is no guidance nor description in the specification in identifying or using sequences that are unique to SEQ ID NO:4 as compared to those known in the prior art. Applicant respectfully disagrees.

The specification as originally filed provides guidance in identifying and using sequences that are unique to SEQ ID NO:4 (human Cyr61) for the preparation of antibodies that are specific to SEQ ID NO:4. For example, lines 3-17 of page 53 state the following:

> The generation of anti-Cyr61 antibodies specific for human Cyr61, for example, is optimized by designing appropriate antigens. The human Cyr61 protein is 381 amino acids long, including the N-terminal secretory signal. As described above, human Cyr61 exhibits a 91% amino acid sequence identity with the 379 amino acid sequence of the mouse protein. However, the mouse and human proteins diverge most significantly in the central portion of the proteins, where they are devoid of cysteines (see above). ***These sequence differences are exploited to elicit antibodies specific to the human Cyr61 by using as an antigen a peptide having a sequence derived from one of the divergent regions in the human protein*** ...

The specification thus provides guidance to one of ordinary skill in the art to produce antibodies specific to SEQ ID NO:4 by using a peptide of human Cyr61 with a sequence different from a corresponding region of mouse Cyr61. One of ordinary skill in the art may readily identify appropriate antigenic peptides by comparing the amino acid sequence of mouse

and human Cyr61 presented in SEQ ID NOS: 2 and 4, respectively. In addition, lines 12-25 of page 45 provide the following guidance:

> The murine Cyr61 protein has a Mr of 41,000 and is 379 amino acids long including the N-terminal secretory signal. There is 91% amino acid sequence identity with the 381 amino acid sequence of the human protein. ... However, the mouse and human proteins do diverge significantly in the central portion of the proteins, where each protein is devoid of cysteines. See, O'Brien et al., Cell Growth & Diff. 3:645-654 (1992). A cysteine-free region in the murine Cyr61 amino acid sequence is found between amino acid residues 164 to 226 (SEQ ID NO:2). A corresponding cysteine-free region is found in the human Cyr61 amino acid sequence between amino acid residues 163 to 229 (SEQ ID NO: 4). More particularly, the mouse and human Cyr61 proteins are most divergent between Cyr61 amino acids 170-185 and 210-225.

The above citations from the specification clearly provide the necessary guidance to allow one of ordinary skill in the art to select appropriate antigens that may be used to produce antibodies that are specific to SEQ ID NO:4. In view of the cited references failing to disclose antibodies that *specifically* bind to human Cyr61 and the guidance provided by the specification in selecting appropriate antigens to produce such antibodies, Applicant respectfully requests reconsideration and withdrawal of the the rejection under 35 U.S.C. § 102(b).

c. 35 U.S.C. § 103(a)

The Examiner has rejected claims 65 and 67-77 as obvious over O'Brien or Yang in view of Hoogenboom. Applicant respectfully submits that the prior art references are insufficient to establish a prima facie case of obviousness because the cited references do not contain each and every element of the claims as amended.

As described above, O'Brien and Yang do not disclose the claimed antibodies that specifically bind to a polypeptide comprising a sequence set forth in SEQ ID NO:4. The Examiner characterizes Hoogenboom as teaching methods of making chimeric or humanized antibodies. Therefore, the previously cited references do not teach each and every element of the claims as amended. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejections under 35 U.S.C. § 103(a).

3. Conclusion

In view of the above amendments and remarks, Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect

is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

HOWREY LLP

Dated: July 8, 2005

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